

Substitute for forms 1449A/PTO &amp; 1449B/PTO

# FOURTH INFORMATION DISCLOSURE STATEMENT BY APPLICANT

ATTORNEY'S DKT NO.

032469-001

APPLICATION NO.

~~09/125,963~~ 10759244

APPLICANT

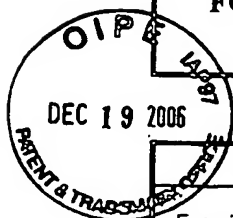
Sam T. LINDHOLM *et al.*

FILING DATE

November 24, 1998

GROUP

1647



## U.S. PATENT DOCUMENTS

Examiner Initials	Document Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Issue/Publication Date (MM-DD-YYYY)
	4,975,527		KOEZUKA <i>et al.</i>	12-04-1990

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Document Number	Kind Code (if known)	Country	Date of Publication (MM-DD-YYYY)	Translation Yes	No
	WO 94/20322		PCT	11-24-1994		
DR	WO 95/24474		PCT	09-14-1995		
DR	WO 95/33830		PCT	12-14-1995		

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
DR	AABOE, M., <i>et al.</i> , "Healing of experimentally created defects: a review," BRITISH JOURNAL OF ORAL & MAXILLOFACIAL SURGERY (1995), pp. 312-318, vol. 33, Churchill Livingstone, Edinburgh, Scotland.
	BODEN, S.D. <i>et al.</i> , "Video-Assisted Lateral Intertransverse Process Arthrodesis," SPINE (1996), pp. 2689-2697, vol. 21, Lippincott Williams & Wilkins, Hagerstown, MD.
	BOSTROM, M., <i>et al.</i> , "Use of Bone Morphogenetic Protein-2 in the Rabbit Ulnar Nonunion Model," CLINICAL ORTHOPAEDICS AND RELATED RESEARCH (1996), pp. 272-282, no. 327, Lippincott Williams & Wilkins, Philadelphia, PA.
	CLEMENT, J.H., <i>et al.</i> , "Bone morphogenetic protein 2 in the early development of <i>Xenopus laevis</i> ," MECHANISMS OF DEVELOPMENT (1995), pp. 357-370, vol. 52, Elsevier Science, Limerick, Ireland.
	COOK, S.D., <i>et al.</i> , "Recombinant Human Bone Morphogenetic Protein-7 Induces Healing in a Canine Long-Bone Segmental Defect Model," CLINICAL ORTHOPAEDICS AND RELATED RESEARCH (1994), pp. 302-312, no. 301, J.B. Lippincott, Philadelphia, PA.
	COOK, S.D., <i>et al.</i> , "The Effect of Recombinant Human Osteogenic Protein-1 on Healing of Large Segmental Bone Defects," THE JOURNAL OF BONE AND JOINT SURGERY, (1994), pp. 827-838, vol. 76-A, Amer. Vol., Boston, MA.
	COOK, S.D., <i>et al.</i> , "In Vivo Evaluation of Recombinant Human Osteogenic Protein (rhOP-1) Implants As a Bone Graft Substitute for Spinal Fusions," SPINE (1994), pp. 1655-1663, vol. 19, Lippincott Williams & Wilkins, Hagerstown, MD.
	COOK, S.D., <i>et al.</i> , "Effect of Recombinant Human Osteogenic Protein-1 on Healing of Segmental Defects in Non-Human Primates," BOSTON JOURNAL OF BONE AND JOINT SURGERY, (1995), pp. 734-750, American ed. 77(5), Boston, MA.
	COOK, S.D., <i>et al.</i> , "Osteogenic Protein-1," CLINICAL ORTHOPAEDICS AND RELATED RESEARCH (1996), pp. 29-38, no. 324, JB Lippincott, Philadelphia, PA.
	DUDLEY, A.T., <i>et al.</i> , "A requirement for bone morphogenetic protein-7 during development of the mammalian kidney and eye," GENES & DEVELOPMENT (1995), pp. 2795-2807, vol. 9, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.
	EHRNBERG, A., <i>et al.</i> , "Comparison of Demineralized Allogeneic Bone Matrix Grafting (the Urist Procedure) and the Ilizarov Procedure in Large Diaphyseal Defects in Sheep," THE JOURNAL OF BONE AND JOINT SURGERY, (1993), pp. 438-447, vol. 11, Orthopaedic Research Society, American Ed. Journal of Bone and Joint Surgery, Boston, MA.
	EINHORN, T.A., <i>et al.</i> , "The Healing of Segmental Bone Defects Induced by Demineralized Bone Matrix," THE JOURNAL OF BONE AND JOINT SURGERY (1984), pp. 274-279, vol. 66-A, The Journal of Bone and Joint Surgery, Boston, MA.
	FANG, J., <i>et al.</i> , "Stimulation of new bone formation by direct transfer of osteogenic plasmid genes," PROC. NATL. ACAD. SCI. (1996), pp. 5753-5758, vol.93 (USA), National Academy of Sciences, Washington, DC.
↓	FISCHGRUND, J.S., <i>et al.</i> , "Augmentation of Autograft Using rhBMP-2 and Different Carrier Media in the Canine Spinal Fusion Model," JOURNAL OF SPINAL DISORDERS (1996), pp. 467-472, vol. 10, No. 6, Lippincott Williams & Wilkins, Hagerstown, MD.
	GAO, T.J. <i>et al.</i> , "Microscopic evaluation of bone-implant contact between hydroxyapatite, bioactive glass and tricalcium phosphate implanted in sheep diaphyseal defects," BIOMATERIALS (1995), pp. 1175-1179, vol. 16, Oxford, England.
	GAO, T.J., <i>et al.</i> , "Enhanced Healing of Segmental Tibial Defects in Sheep by a Composite Bone Substitute Comprised of Tricalcium Phosphate Cylinder, Bone Morphogenetic Protein and Type IV Collagen," JOURNAL OF BIOMEDICAL MATERIALS RESEARCH (1996), vol. 32, Interscience, Wiley, Hoboken, NJ.
	GAO, T.J. <i>et al.</i> , "A coral composite implant containing bone morphogenetic protein repairs a segmental tibial defect in sheep: mechanics and immune assay," INTERNATIONAL ORTHOPAEDICS., German Ceramics Society, Cologne, Germany.
	GAO, T.J. <i>et al.</i> , "Comparative Study on Potential of Natural Coral and Tricalcium Phosphate Cylinders in Healing a Segmental Diaphyseal Defect in Sheep," BIO-CERAMICS, pp. 199-204, vol. 8, German Ceramics Society, Cologne, Germany.
	GAO, T.J., <i>et al.</i> , "Composite of Bone Morphogenetic Protein (BMP) and Type IV Collagen, Coral-Derived Coral Hydroxyapatite and Tricalcium Phosphate Ceramics," INTERNATIONAL ORTHOPAEDICS (ACCEPTED), Springer Verlag, Berlin, Germany.

Substitute for forms 1449A/PTO & 1449B/PTO  <b>FOURTH INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	ATTORNEY'S DKT NO. 032469-001	APPLICATION NO. <del>097123,965</del> 10759244
	APPLICANT Sam T. LINDHOLM <i>et al.</i>	
	FILING DATE November 24, 1998	GROUP 1647

NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
	GAO, T.J., et al., "Bone Inductive Potential and Dose-Dependent Response of Bovine Bone Morphogenetic Protein Combined with Type IV Collagen Carrier," <i>ANNALES CHIRURGIAE ET GYNAECOLOGIAE</i> (1993), pp. 77-84, vol. 207, University of Tampere, Finland, University of Helsinki, Finland.
DR	GERHART, T.N., et al., "Healing Segmental Femoral Defects in Sheep Using Recombinant Human Bone Morphogenetic Protein," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1993), pp. 317-326, no. 293, J.B. Lippincott Company, Philadelphia, PA.
	HECKMAN, J.D., et al., "The Use of Bone Morphogenetic Protein in the Treatment of Non-Union in a Canine Model," <i>THE JOURNAL OF BONE AND JOINT SURGERY</i> (1991), pp. 750-764, vol. 73-A, The Journal of Bone and Joint Surgery, American Volume, Boston, MA.
	HELM, G.A., et al., "Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous one lumbar spinal fusion," <i>J. NEUROSURGERY</i> , (1997), pp. 93-100, vol. 86, Charlottesville, VA.
	HOGAN, B.L.M., "Bone morphogenetic proteins: multifunctional regulators of vertebrate development," <i>GENES &amp; DEVELOPMENT</i> (1996), pp. 1580-1594, vol. 10, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.
	HOLLIGER, E.H., et al., "Morphology of the Lumbar Intertransverse Process Fusion Mass in the Rabbit Model: A Comparison Between Two Bone Graft Materials — rhBMP-2 and Autograft," <i>JOURNAL OF SPINAL DISORDERS</i> (1996), pp. 125-128, vol. 9, Lippincott Williams & Wilkins, Hagerstown, MD.
	HOLLINGER, J. & LEONG, K., "Poly( $\alpha$ -hydroxy acids): carriers for bone morphogenetic proteins," <i>BIOMATERIALS</i> (1996), pp. 187-194, vol. 17, Elsevier Science Limited, Butterworth-Heinemann, Oxford, England.
	HOTZ, G. & HARR, G., "Bone substitute with osteoinductive biomaterials — current and future clinical applications," <i>INT. J. ORAL MAXILLOFAC. SURG.</i> (1994), pp. 413-417, vol. 23, Munksgaard, Copenhagen, Denmark
	HU, Y.Y., "Experimental studies on reconstituted xenograft and its clinical application," <i>Chinese Journal of Surgery</i> , Vol. 31, no. 12, pp. 709-713, Zhonghua yi xue hui, Wai ke xue hui, Beijing, China.
	JOHNSON, E.E. & URIST, M.R., "Distal Metaphyseal Tibial Nonunions Associated with Significant Bowing Deformity and Cortical Bone Loss: Treatment with Human Bone Morphogenetic Protein (h-BMP) and Internal Fixation," (1989), pp. 613-620, vol. 63, Nippon Seikeigeka Gakkai Zasshi, Japan.
	JOHNSON, E.E., et al., "Repair of Segmental Defects of the Tibia with Cancellous Bone Grafts Augmented with Human Bone Morphogenetic Protein," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1988), pp. 249-257, no. 236, JB Lippincott, Philadelphia, PA.
	JOHNSON, E.E., et al., "Bone Morphogenetic Protein Augmentation Grafting of Resistant Femoral Nonunions," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1988), pp. 257-265, no. 230, JB Lippincott, Philadelphia, PA.
	JOHNSON, E.E., et al., "Autogenic Cancellous Bone Grafts in Extensive Segmental Ulnar Defects in Dogs," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1989), pp. 254-265, no. 243, JB Lippincott, Philadelphia, PA.
	KATO, F., "Experimental study of chemical spinal fusion in the rabbit by means of bone morphogenetic protein," (1990), PubMed 2380596, Nippon Seikeigeka Gakkai Zasshi, Japan.
	KUBOKI, Y., et al., "Two Distinctive BMP-Carriers Induce Zonal Chondrogenesis and Membranous Ossification, Respectively: Geometrical Factors of Matrices for Cell-Differentiation," <i>CONNECTIVE TISSUE RESEARCH</i> (1995), pp. 219-226, vol. 32, Taylor & Francis, Philadelphia, PA.
	LEE, S.C., et al., "Healing of large segmental defects in rat femurs is aided by RhBMP-2 in PLGA matrix," <i>JOURNAL OF BIOMEDICAL MATERIALS RESEARCH</i> (1994), pp. 1149-1156, vol. 28, Wiley Interscience, Hoboken, NJ.
	LINDE, A. and HEDNER, E., "Recombinant Bone Morphogenetic Protein-2 Enhances Bone Healing, Guided by Osteopromotive e-PTFE Membranes: An Experimental Study in Rats," <i>CALCIFIED TISSUE INT.</i> (1995), pp. 549-553, vol. 56, Springer-Verlag, NY.
	LINDHOLM, T.S., et al., "Response of Bone Marrow Stroma Cells to Demineralized Cortical Bone Matrix in Experimental Spinal Fusion in Rabbits," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1988), pp. 296-302, no. 230, JB Lippincott, Philadelphia, PA.
↓	LINDHOLM, T.C., et al., "Bone Morphogenetic Proteins Regenerating Skull and Maxillo-Mandibular Defects," <i>BONE MORPHOGENETIC PROTEINS</i> (1996), pp. 149-155, R.G. Landes Company, Austin, TX.
	<del>LINDHOLM, T.S. and GAO, T.J., "Functional Carriers for Bone Morphogenetic Proteins," <i>ANNALES CHIRURGIAE ET GYNAECOLOGIAE Supplementum</i>, (1993), pp. 3-12, vol. 82, University of Helsinki, Helsinki, Finland.</del>
DR	LOVELL, T.P., et al., "Augmentation of Spinal Fusion With Bone Morphogenetic Protein in Dogs," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1989), pp. 266-274, no. 243, JB Lippincott, Philadelphia, PA.
↓	MIYAMOTO, S. & TAKAOKA, K., "Bone Induction and Bone Repair by Composites of Bone Morphogenetic Protein and Biodegradable Synthetic Polymers," <i>ANNALES CHIRURGIAE ET GYNAECOLOGIAE Supplement</i> , 69-76, vol. 82, University of Helsinki, Helsinki, Finland.
	MUSCHLER, G.F., et al., "Evaluation of Human Bone Morphogenetic Protein 2 in a Canine Spinal Fusion Model," <i>CLINICAL ORTHOPAEDICS AND RELATED RESEARCH</i> (1994), pp. 229-240, no. 308, J.B. Lippincott Company, Philadelphia, PA.
↓	NILSSON, O.S., et al., "Bone Repair Induced by Bone Morphogenetic Protein in Ulnar Defects in Dogs," <i>THE JOURNAL OF BONE AND JOINT SURGERY</i> , British Volume, (1986), pp. 635-642, vol. 68-B, London, UK.

Substitute for forms 1449A/PTO &amp; 1449B/PTO

FOURTH INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTATTORNEY'S DKT NO.  
032469-001APPLICATION NO.  
~~09/125,969~~ 10759244APPLICANT  
Sam T. LINDHOLM *et al.*FILING DATE  
November 24, 1998GROUP  
1647

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
DR	ODA, S., et al., "Ectopic bone induction in recombinant human bone morphogenetic protein-2 (rhBMP-2) combined with biphasic calcium phosphate (BCP)," (1996), The Journal of Stomatological Society, Japan
	ONO, I., et al., "Promotion of the Osteogenic Activity of Recombinant Human Bone Morphogenetic Protein by Prostaglandin E <sub>1</sub> ," BONE (1996), pp. 581-588, vol. 19, Elsevier Science Inc., NY.
	PANGANIBAN, G.E.F., et al., "Biochemical Characterization of the <i>Drosophila dpp</i> Protein, a Member of the Transforming Growth Factor $\beta$ Family of Growth Factors," MOLECULAR AND CELLULAR BIOLOGY (1990), pp. 2669-2677, vol. 10, American Society for Microbiology, Washington, DC.
	PETIT, J.C. & RIPAMONTI, U., "Tissue Segregation Enhances Calvarial Osteogenesis in Adult Primates," THE JOURNAL OF CRANIOFACIAL SURGERY (1994), pp. 34-43, vol. 5, Little, Brown & Co., Boston, MA.
	RAGNI, P. & LINDHOLM T.S., "Interaction of Allogeneic Demineralized Bone Matrix and Porous Hydroxyapatite Bioceramics in Lumbar Interbody Fusion in Rabbits," CLINICAL ORTHOPAEDICS AND RELATED RESEARCH (1991), pp. 292-299, no. 272, JB Lippincott, Philadelphia, PA.
	RAGNI, P., et al., "Spinal Fusion Induced by Porous Hydroxyapatite Blocks (HA)," pp. 133-144, Italian Journal of Orthopaedics & Traumatology, Bologna, Italy.
	RAGNI, P.C. & LINDHOLM, T.S., "Bone Formation and Static Changes in the Thoracic Spine at Uni- or Bilateral Experimental Spondylolysis with Demineralized Bone Matrix (DBM)," pp. 237-252, Italian Journal of Orthopaedics & Traumatology, Bologna, Italy.
	RILEY, E.H., et al., "Bone Morphogenetic Protein-2," CLINICAL ORTHOPAEDICS AND RELATED RESEARCH (1996), pp. 39-46, no. 324, JB Lippincott, Philadelphia, PA.
	SAILER, H.F. & KOLB, E., "Application of purified bone morphogenetic protein (BMP) preparations in cranio-maxillo-facial surgery," JOURNAL OF CRANIO-MAXILLO-FACIAL SURGERY (1994), pp. 191-199, vol. 22, Churchill Livingstone, Edinburgh, Scotland.
	SAILER, H.F. & KOLB, E., "Application of purified bone morphogenetic protein (BMP) in cranio-maxillo-facial surgery," JOURNAL OF CRANIO-MAXILLO-FACIAL SURGERY (1994), pp. 2-11, vol. 22, Churchill Livingstone, Edinburgh, Scotland.
	<del>SAMPATH, T.K. &amp; REDDI, A.H., "Homology of bone inductive proteins from human, monkey, bovine, and rat extracellular matrix," PROC. NATL. ACAD. SCI. USA (1983), pp. 6591-6595, vol. 80, National Academy of Sciences, Washington, DC.</del>
DR	SAMPATH, T.K., et al., " <i>Drosophila</i> transforming growth factor $\beta$ superfamily proteins induce endochondral bone formation in mammals," PROC. NATL. ACAD. SCI. USA (1993), pp. 6004-6008, vol. 90, National Academy of Sciences, Washington, DC.
	SANDHU, H.S., et al., "Evaluation of rhBMP-2 With an OPLA Carrier in a Canine Posterolateral (Transverse Process) Spinal Fusion Model," SPINE (1995), pp. 2669-2683, vol. 20, Lippincott-Raven Publishers
	SANDHU, H.S., et al., "Effective Doses of Recombinant Human Bone Morphogenetic Protein-2 in Experimental Spinal Fusion," SPINE (1996), pp. 2115-2122, vol. 21, Lippincott Williams & Wilkins, Hagerstown, MD.
	SCHIMANDLE, J.H., et al., "Experimental Spinal Fusion With Recombinant Human Bone Morphogenetic Protein-2," SPINE (1995), pp. 1326-1337, vol. 20, Lippincott Williams & Wilkins, Hagerstown, MD.
	SHEEHAN, J.P., et al., "Molecular Methods of Enhancing Lumbar Spine Fusion," NEUROSURGERY (1996), pp. 548-554, vol. 39
	STAEHLING-HAMPTON, K., et al., "Specificity of Bone Morphogenetic Protein-related Factors: Cell Fate and Gene Expression Changes in <i>Drosophila</i> Embryos Induced by <i>decapentaplegic</i> but not 60A," CELL GROWTH & DIFFERENTIATION (1994), pp. 585-593, vol. 5, American Association for Cancer Research, Philadelphia, PA.
	SUN, Y., et al., "Repair of large cranial defect using allogeneic cranial bone and bone morphogenetic protein," PUBMED 7600438 (1995), Chinese Journal of Plastic Surgery and Burns, Beijing, China.
	TORIUMI, D.M., et al., "Mandibular Reconstruction With a Recombinant Bone-Inducing Factor," ARCH OTOLARYNGOL HEAD NECK SURG (1991), pp. 1101-1112, vol. 117, American Medical Association, Chicago, IL.
	URIST, M.R., et al., "Regeneration of an enchondroma defect under the influence of an implant of human bone morphogenetic protein," THE JOURNAL OF HAND SURGERY (1986), pp. 417-419, Vol. 11A, Churchill Livingstone, Secaucus, NJ.
	VAN EEDEN, S.P. & RIPAMONTI, U., "Bone Differentiation in Porous Hydroxyapatite in Baboons Is Regulated by the Geometry of the Substratum: Implications for Reconstructive Craniofacial Surgery," PLASTIC AND RECONSTRUCTIVE SURGERY (1994), pp. 959-966, vol. 93, Lippincott Williams & Wilkins, Hagerstown, MD.
	<del>VILJANEN, V.V., et al., "Partial Purification and Characterization of Bone Morphogenetic Protein from Bone Matrix of the Premature Mouse (<i>Aves alces</i>): Degradation of Bone-Inducing Activity during Storage," (1996), pp. 447-460, vol. 20, European Surgical Research, Karger, Basel, Switzerland.</del>
DR	VILJANEN, V.V., "Allogeneic and xenogeneic bone morphogenetic protein in skeletal reconstruction," (Academic Dissertation) UNIVERSITY OF TAMPERE (1997), Tampere, Finland
	WHARTON, K.A., et al., " <i>Drosophila</i> 60A gene, another transforming growth factor $\beta$ family member, is closely related to human bone morphogenetic proteins," PROC. NATL. ACAD. SCI. USA (1991), pp. 9214-9218, vol. 88, National Academy of Sciences, Washington, DC.
	WOLFE M.W. & COOK, S.D., "Use of osteoinductive implants in the treatment of bone defects," MEDICAL PROGRESS THROUGH TECHNOLOGY (1994), pp. 155-168, vol. 20, Kluwer Academic, Boston, MA.

Substitute for forms 1449A/PTO & 1449B/PTO		ATTORNEY'S DKT NO. 032469-001	APPLICATION NO. <del>09/123,905</del> 10759244
FOURTH INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT Sam T. LINDHOLM <i>et al.</i>	
		FILING DATE November 24, 1998	GROUP 1647

NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Include name of author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
DR	YASKO, A.W., et al., "The Healing of Segmental Bone Defects, Induced by Recombinant Human Bone Morphogenetic Protein (rhBMP-2)," THE JOURNAL OF BONE AND JOINT SURGERY, (1992), pp. 639-670, vol. 74-A, American Ed. Journal of Bone and Joint Surgery, Boston, MA.

Examiner Signature	/David Romeo/ (01/11/2007)	Date Considered	
-----------------------	----------------------------	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with M.P.E.P. § 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.